09758917

(FILE 'HOME' ENTERED AT 12:49:51 ON 19 MAR 2004)

FILE 'MEDLINE' ENTERED AT 12:50:03 ON 19 MAR 2004
L1 1347 S THROUGHPUT SCREENING
L2 5 S L1 AND PAIN

=> s l1 and py<1996
10559736 PY<1996
L3 18 L1 AND PY<1996

=> d 1-18 bib abs kwic

L3 ANSWER 1 OF 18 MEDLINE on STN
AN 97059645 MEDLINE
DN PubMed ID: 8903966
TI Challenges of high **throughput screening** against cell surface receptors.
AU Major J S
CS ZENECA Pharmaceuticals, Macclesfield, Cheshire, UK.
SO Journal of receptor and signal transduction research, **(1995 Jan-Mar)** 15 (1-4) 595-607. Ref: 5
Journal code: 9509432. ISSN: 1079-9893.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199703
ED Entered STN: 19970321
Last Updated on STN: 19970321
Entered Medline: 19970312
AB Excessive or inappropriate activation of cell surface receptors can mediate the development of disease. Receptors, therefore, are a focus for drug discovery activities. Empirical screening is important in the search for novel compounds acting as receptors. Technical developments and the application of molecular biology have facilitated access to receptors of interest and have provided efficient screening methods capable of very high throughput. Reliability in high **throughput screening** requires the use of appropriate methodology, good screen design and effective validation and quality control processes. Validation should aim to establish that the basic experimental design is sound. In developing software to handle high **throughput screening** data, a fundamental requirement is to provide performance monitoring and error trapping facilities. Additional requirements are automatic data capture from instruments, on-line data reduction and analysis and transfer of results to central databases. As data volumes increase through effective high **throughput screening,** conventional interrogation methods become less appropriate and are being augmented by newer computing techniques referred to as knowledge mapping or database mining. Targeting cell surface receptors has been very successful as an approach to drug discovery. If the challenges of high throughput empirical screening are addressed effectively, cell surface receptors will provide new opportunities for improved therapy in the coming years.
TI Challenges of high **throughput screening** against cell surface receptors.
SO Journal of receptor and signal transduction research, **(1995 Jan-Mar)** 15 (1-4) 595-607. Ref: 5
Journal code: 9509432. ISSN: 1079-9893.
AB . . . facilitated access to receptors of interest and have provided efficient screening methods capable of very high throughput. Reliability in high **throughput screening** requires the use of appropriate methodology, good screen design and effective validation and quality control processes. Validation should aim to establish that the basic experimental design is sound. In developing software to handle high **throughput screening** data, a fundamental requirement is to provide performance monitoring and error trapping facilities. Additional requirements are automatic data capture from. . . instruments, on-line data reduction and analysis and transfer of results to central databases. As data volumes increase through effective high **throughput screening,** conventional interrogation methods become less appropriate and are being augmented by newer computing techniques referred to as knowledge mapping or. . .

L3 ANSWER 2 OF 18 MEDLINE on STN
AN 96359707 MEDLINE

09758917

DN PubMed ID: 8747472
TI Quantitative determination of DNA-binding parameters for the human estrogen receptor in a solid-phase, nonseparation assay.
AU Carlsson B; Haggblad J
CS Karo Bio AB, Novum, Huddinge, Sweden.
SO Analytical biochemistry, **(1995 Dec 10)** 232 (2) 172-9.
Journal code: 0370535. ISSN: 0003-2697.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199610
ED Entered STN: 19961106
Last Updated on STN: 19980206
Entered Medline: 19961024
AB Binding of transcription factors to specific sequences of DNA has been studied for more than a decade and has become a very productive field of research. This paper describes the application of the recently developed technique of scintillating microtitration plates in the study of protein-DNA interactions. A DNA sequence containing the classical consensus estrogen response element derived from the 5' upstream regulatory region of the frog vitellogenin gene was immobilized to scintillating microtitration plates. Equilibrium binding studies and kinetic studies were performed with [3H] estradiol labeled human estrogen receptor. The observed equilibrium dissociation constant (Kd) was 2.0 +/- 0.3 nM and the observed Hill coefficient of 2.0 indicated a positive cooperativity. Two association rate constants were observed, one slower of 0.3 x 10(6) M-1 min-1 for lower concentrations of estrogen receptor and one faster of 6.3 x 10(6) M-1 min-1 for higher concentrations. The dissociation rate was 0.005 min-1. The technique described has a potential in basic research concerning characterization of DNA binding. It is also well suited to applied research as a tool in high-**throughput screening** of compound libraries in the search of agents inhibiting transcription factor binding to DNA.
SO Analytical biochemistry, **(1995 Dec 10)** 232 (2) 172-9.
Journal code: 0370535. ISSN: 0003-2697.
AB . . . in basic research concerning characterization of DNA binding. It is also well suited to applied research as a tool in high-**throughput screening** of compound libraries in the search of agents inhibiting transcription factor binding to DNA.

L3 ANSWER 3 OF 18 MEDLINE on STN
AN 96099907 MEDLINE
DN PubMed ID: 7503425
TI Soluble interleukin-5 receptor alpha-chain binding assays: use for screening and analysis of interleukin-5 mutants.
AU Banks M; Graber P; Proudfoot A E; Arod C Y; Allet B; Bernard A R; Sebille E; McKinnon M; Wells T N; Solari R
CS Department of New Lead Discovery, Glaxo Wellcome Medicines Research Centre, Stevenage, Hertfordshire, United Kingdom.
SO Analytical biochemistry, **(1995 Sep 20)** 230 (2) 321-8.
Journal code: 0370535. ISSN: 0003-2697.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199601
ED Entered STN: 19960217
Last Updated on STN: 19960217
Entered Medline: 19960118
AB Interleukin-5 (IL-5) is a key cytokine for the production, differentiation, and activation of eosinophils. IL-5 is a member of the four helical bundle family of cytokines, and in common with many members of the cytokine family it binds to a heterodimeric receptor composed of a ligand binding alpha-chain and a signal-transducing beta-chain. We have established two receptor/ligand binding assays based on the extracellular domain of the receptor alpha-chain which we have produced as a fusion protein. One assay is based on scintillation proximity fluoromicrospheres and radiolabeled ligand and the other on detection of biotinylated ligand binding to immobilized receptor using a chemiluminescent substrate in a 96-well microtiter plate format. Both receptor binding assays have been optimized for high **throughput screening** for receptor antagonists. These assays were also used for analytical purposes and the binding of ligand to the receptor alpha-chain was compared directly to receptor binding assays performed on TF-1 cells which express the receptor alpha beta-heterodimer. These three assays have been used to study

site-directed mutants of IL-5 to determine the important residues for interaction of the cytokine with each chain of the receptor (P. Graber et al. (1995) J. Biol. Chemical 270, 15762-15769).
SO Analytical biochemistry, **(1995 Sep 20)** 230 (2) 321-8.
Journal code: 0370535. ISSN: 0003-2697.
AB . . . receptor using a chemiluminescent substrate in a 96-well microtiter plate format. Both receptor binding assays have been optimized for high **throughput screening** for receptor antagonists. These assays were also used for analytical purposes and the binding of ligand to the receptor alpha-chain. . .

L3 ANSWER 4 OF 18 MEDLINE on STN
AN 96082502 MEDLINE
DN PubMed ID: 7581857
TI Biological and biophysical characterization of recombinant soluble human E-selectin purified at large scale by reversed-phase high-performance liquid chromatography.
AU Burrows S D; Franklin S G; Brigham-Burke M R; Brooks I S; McNulty D E; Feild J A; Anumula K R; O'Shannessy D J
CS Department of Protein Biochemistry, SmithKline Beecham Pharmaceuticals, King of Prussia, PA 19406-0939, USA.
SO Journal of chromatography. B, Biomedical applications, **(1995 Jun 23)** 668 (2) 219-31.
Journal code: 9421796. ISSN: 0378-4347.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199512
ED Entered STN: 19960124
Last Updated on STN: 19970203
Entered Medline: 19951212
AB A first step in the development of a high-**throughput screening** assay for antagonists of human E-selectin is the purification and characterization of the selectin. In the present paper we describe a single-step, rapid, reversed-phase HPLC purification protocol for the recombinant, soluble form of human E-selectin (rshE-selectin) produced in Chinese hamster ovary cells. The procedure resulted in high protein yields with recoveries of greater than 98%. Characterization of the reversed-phase purified rshE-selectin showed this product to be analogous to rshE-selectin purified using conventional chromatographic techniques with respect to biological activity and molecular shape. However, the carbohydrate composition of reversed-phase purified rshE-selectin, which had been variable with conventionally purified material, was found to be constant across several isolations. The protocol described herein eliminated the high mannose component associated with previously purified rshE-selectin and provided a uniform carbohydrate composition for additional experimental studies, such as NMR. This fact, coupled with the high yield and simplicity of the present purification scheme are distinct advantages over those previously published. It is expected that other mammalian selectins, such as P-selectin and L-selectin, would also be amenable to reversed-phase HPLC purification.
SO Journal of chromatography. B, Biomedical applications, **(1995 Jun 23)** 668 (2) 219-31.
Journal code: 9421796. ISSN: 0378-4347.
AB A first step in the development of a high-**throughput screening** assay for antagonists of human E-selectin is the purification and characterization of the selectin. In the present paper we describe. . .

L3 ANSWER 5 OF 18 MEDLINE on STN
AN 96059190 MEDLINE
DN PubMed ID: 7482989
TI Fishing for drugs from the sea: status and strategies.
AU de Vries D J; Beart P M
CS Department of Pharmacology, University of Otago, Dunedin, New Zealand.
SO Trends in pharmacological sciences, **(1995 Aug)** 16 (8) 275-9.
Journal code: 7906158. ISSN: 0165-6147.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199511
ED Entered STN: 19960124
Last Updated on STN: 19960124

Entered Medline: 19951124
AB Marine organisms represent an enormous, essentially unexploited, resource of natural products. Globally, the race to develop marine-derived drugs is well under way with many pharmaceutical companies positioning themselves to reap large profits by the exploitation of the ocean's rich chemical diversity. Targeted strategies, often in combination with high-**throughput screening**, are being employed in this hunt for novel pharmacotherapeutic agents. David de Vries and Phil Beart examine the potential, problems and technologies of an international pharmaceutical search that has important ethical considerations.
SO Trends in pharmacological sciences, **(1995 Aug)** 16 (8) 275-9.
Journal code: 7906158. ISSN: 0165-6147.
AB . . . themselves to reap large profits by the exploitation of the ocean's rich chemical diversity. Targeted strategies, often in combination with high-**throughput screening**, are being employed in this hunt for novel pharmacotherapeutic agents. David de Vries and Phil Beart examine the potential, problems. . .

L3 ANSWER 6 OF 18 MEDLINE on STN
AN 96050146 MEDLINE
DN PubMed ID: 7501686
TI Strategies and recent technologies in drug discovery.
AU Kubinyi H
CS Drug Design, BASF, Ludwigshafen.
SO Die Pharmazie, **(1995 Oct)** 50 (10) 647-62. Ref: 311
Journal code: 9800766. ISSN: 0031-7144.
CY GERMANY: Germany, Federal Republic of
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 199601
ED Entered STN: 19960217
Last Updated on STN: 19960217
Entered Medline: 19960116
AB In the last years, the paradigms of drug research changed significantly. New technologies were developed, in several different fields. Combinatorial chemistry and high-**throughput screening** increase our chances to find new lead structures, with less effort than by dedicated syntheses. Gene technology, in addition to providing therapeutically useful proteins, significantly contributes to rational drug design. The primary structure of a protein can be derived from the DNA sequence of the corresponding gene. Its relevance for a certain disease is investigated in transgenic animals. Expression of the protein in bacteria or in cell culture produces material for screening systems and for 3D structure determination by protein crystallography. NMR techniques, or electron cryo-microscopy. Structure-based and computer-aided design methods are applied to optimize lead structures with the least effort. A serious problem in the application of such techniques is their limitation to ligand-protein interactions. For the design of a therapeutically useful drug, also absorption, distribution, metabolism and elimination have to be considered. QSAR methods help in this respect. Scope and limitations of the new technologies are discussed in the context of conventional approaches in drug discovery.
SO Die Pharmazie, **(1995 Oct)** 50 (10) 647-62. Ref: 311
Journal code: 9800766. ISSN: 0031-7144.
AB . . . last years, the paradigms of drug research changed significantly. New technologies were developed, in several different fields. Combinatorial chemistry and high-**throughput screening** increase our chances to find new lead structures, with less effort than by dedicated syntheses. Gene technology, in addition to. . .

L3 ANSWER 7 OF 18 MEDLINE on STN
AN 95393927 MEDLINE
DN PubMed ID: 7664692
TI A rapid and sensitive binding assay for growth hormone releasing factor.
AU Carrick T A; Bingham B; Eppler C M; Baumbach W R; Zysk J R
CS Molecular & Cellular Biology Group, Agricultural Research Center, American Cyanamid Company, Princeton, New Jersey 08543, USA.
SO Endocrinology, **(1995 Oct)** 136 (10) 4701-4.
Journal code: 0375040. ISSN: 0013-7227.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Abridged Index Medicus Journals; Priority Journals

09758917

EM 199510
ED Entered STN: 19951020
Last Updated on STN: 19951020
Entered Medline: 19951012
AB A binding assay for growth hormone releasing factor (GRF) has been developed using scintillation proximity assay (SPA) technology. Binding conditions were validated by several criteria. Equilibrium binding was attained within three hours at 22 degrees C in crude membrane fractions of HEK293 (293-P2) and GH4C1 (GH4-P1) cells transfected with the porcine GRF receptor. Saturation binding isotherms produced a KD of 296 pM and a Bmax of 4.7 pmols/mg membrane protein in 293-P2 cells. Cells not expressing the GRF receptor displayed no specific binding for the ligand. Competition binding curves produced the following rank order of potency for tested peptides: GRF analogs D-Ala2 = D-Arg2 (IC50 approximately 1 nM) >> PACAP > secretin, VIP (EC50 > 100 nM). Somatostatin (SRIF) binding was also adapted to the SPA format in a GH4C1 cell line transfected with the SRIF receptor subtype 2 (SSTR2) and in HEK293 cells transfected with the SRIF receptor subtype 5 (SSTR5). This assay represents a major improvement for binding measurements of these and potentially many other ligands for G-protein linked receptors, requiring no separation of bound from free hormone, allowing detailed pharmacological evaluations and enabling measurement of equilibrium binding in real time. In the 96-well format, it is suitable for high **throughput screening**.
SO Endocrinology, **(1995 Oct)** 136 (10) 4701-4.
Journal code: 0375040. ISSN: 0013-7227.
AB . . . pharmacological evaluations and enabling measurement of equilibrium binding in real time. In the 96-well format, it is suitable for high **throughput screening**.

L3 ANSWER 8 OF 18 MEDLINE on STN
AN 95327658 MEDLINE
DN PubMed ID: 7541541
TI Liquid-phase combinatorial synthesis.
AU Han H; Wolfe M M; Brenner S; Janda K D
CS Department of Molecular Biology, Scripps Research Institute, La Jolla, CA 92037, USA.
SO Proceedings of the National Academy of Sciences of the United States of America, **(1995 Jul 3)** 92 (14) 6419-23.
Journal code: 7505876. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199508
ED Entered STN: 19950822
Last Updated on STN: 19960129
Entered Medline: 19950810
AB A concept termed liquid-phase combinatorial synthesis (LPCS) is described. The central feature of this methodology is that it combines the advantages that classic organic synthesis in solution offers with those that solid-phase synthesis can provide, through the application of a linear homogeneous polymer. To validate this concept two libraries were prepared, one of peptide and the second of nonpeptide origin. The peptide-based library was synthesized by a recursive deconvolution strategy [Erb, E., Janda, K. D. & Brenner, S. (1994) Proc. Natl. Acad. Sci. USA 91, 11422-11426] and several ligands were found within this library to bind a monoclonal antibody elicited against beta-endorphin. The non-peptide molecules synthesized were arylsulfonamides, a class of compounds of known clinical bactericidal efficacy. The results indicate that the reaction scope of LPCS should be general, and its value to multiple, high-**throughput screening** assays could be of particular merit, since multimilligram quantities of each library member can readily be attained.
SO Proceedings of the National Academy of Sciences of the United States of America, **(1995 Jul 3)** 92 (14) 6419-23.
Journal code: 7505876. ISSN: 0027-8424.
AB . . . clinical bactericidal efficacy. The results indicate that the reaction scope of LPCS should be general, and its value to multiple, high-**throughput screening** assays could be of particular merit, since multimilligram quantities of each library member can readily be attained.

L3 ANSWER 9 OF 18 MEDLINE on STN
AN 95252099 MEDLINE
DN PubMed ID: 7537523
TI Induction and relief of nasal congestion in ferrets infected with

influenza virus.
AU Chen K S; Bharaj S S; King E C
CS Procter & Gamble Pharmaceutical Research Division, Miami Valley Laboratories, Procter & Gamble Company, Cincinnati, Ohio 45253-8707, USA.
SO International journal of experimental pathology, **(1995 Feb)** 76 (1) 55-64.
Journal code: 9014042. ISSN: 0959-9673.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199506
ED Entered STN: 19950615
Last Updated on STN: 19960129
Entered Medline: 19950602
AB Susceptible ferrets intranasally infected with influenza virus consistently responded with maximal nasal secretion of virus, febrile reaction, and influx of inflammatory cells into nasal lumen on day 2 post infection (d.p.i.). Polymorphonuclear leucocytes were the earliest predominant cell, followed by monocytes/macrophages while lymphocytes were maintained as a minor population throughout the 7-day period. Nasal congestion level, continuously monitored by computer aided active anterior rhinomanometry, was reproducibly maximal at 2 d.p.i., diminished in intensity the next day and returned to the basal level within 7 d.p.i. Nasal congestion was effectively relieved by a single intranasal dose of 0.1% oxymetazoline or 0.2% phenylephrine, or a single intragastric administration of pseudoephedrine. Intranasal delivery of a single dose of 1% pyrilamine relieved nasal congestion while 0.8% ipratropium bromide and 30% cimetidine were ineffective. These results suggested that nasal congestion is regulated by alpha-adrenergic receptors in the mucosal vasculature or by H1 histamine receptor, but is unaffected by inhibitors of nasal secretion regulated by the cholinergic nervous system. The present study indicates that the infectious rhinitis ferret model provides a reproducible nasal congestion pattern that can be objectively measured by a refined active anterior rhinomanometric system. This labour intensive measurement, however, makes it difficult either to conduct a large population animal study or to use it for a rapid **throughput screening** of new drugs. The temporal relation between the influx of inflammatory cells into the nasal lumen and the onset of nasal congestion underlies the model's relevance to the exploration of the pathogenic mechanism(s) during viral rhinitis.
SO International journal of experimental pathology, **(1995 Feb)** 76 (1) 55-64.
Journal code: 9014042. ISSN: 0959-9673.
AB . . . measurement, however, makes it difficult either to conduct a large population animal study or to use it for a rapid **throughput screening** of new drugs. The temporal relation between the influx of inflammatory cells into the nasal lumen and the onset of. . .

L3 ANSWER 10 OF 18 MEDLINE on STN
AN 94182744 MEDLINE
DN PubMed ID: 8135370
TI Discovery and analysis of a series of C2-symmetric HIV-1 proteinase inhibitors derived from penicillin.
AU Gray N M; Cameron J M; Cammack N; Cobley K N; Holmes D S; Humber D C; Orr D C; Penn C R; Potter R; Madar S; +
CS Department of Virology, Glaxo Group Research Ltd., Greenford, Middlesex, United Kingdom.
SO Analytical biochemistry, **(1994 Jan)** 216 (1) 89-96.
Journal code: 0370535. ISSN: 0003-2697.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; AIDS
EM 199404
ED Entered STN: 19940428
Last Updated on STN: 19970203
Entered Medline: 19940418
AB In order to identify a suitable peptide substrate for human immunodeficiency virus-1 (HIV-1) proteinase, a range of peptides from various cleavage sites within the gag-pol polyprotein were assayed by HPLC for specific cleavage. The peptide with the optimal combination of favorable kinetics and good solubility was based on the N-terminus cleavage site of HIV-1 proteinase (KQGTVSFNF*PQIT). The HPLC assay, using the above peptide, was developed into a rapid isocratic method in order to analyze inhibition kinetics. An assay suitable for high-

throughput screening was developed using a radioactively labeled peptide with the same sequence, coupled to a solid phase. Using this assay, a C2-symmetric HIV-1 proteinase inhibitor derived from penicillin was discovered during random screening of a compound library. A chemical synthesis program developed this structure into a series of potent inhibitors. The lead structures were highly selective for HIV-1 proteinase with good antiviral activity in vitro against HIV and no cytotoxicity. The HPLC assay was used to demonstrate that these compounds are competitive tight-binding inhibitors of HIV-1 proteinase.

SO Analytical biochemistry, **(1994 Jan)** 216 (1) 89-96.
Journal code: 0370535. ISSN: 0003-2697.

AB . . . the above peptide, was developed into a rapid isocratic method in order to analyze inhibition kinetics. An assay suitable for high-**throughput screening** was developed using a radioactively labeled peptide with the same sequence, coupled to a solid phase. Using this assay, a. . .

L3 ANSWER 11 OF 18 MEDLINE on STN
AN 94079811 MEDLINE
DN PubMed ID: 8257635
TI A quantitative assay for trans-activation by HIV-1 Tat, using liposome-mediated DNA uptake and a parallel ELISA system.
AU Watson M E; Moore M
CS Xenova Limited, Slough, Berkshire, England.
SO AIDS research and human retroviruses, **(1993 Sep)** 9 (9) 861-7.
Journal code: 8709376. ISSN: 0889-2229.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; AIDS
EM 199401
ED Entered STN: 19940203
Last Updated on STN: 19970203
Entered Medline: 19940119
AB A cellular assay is described in which transient high-level expression of a heterologous reporter gene (chloramphenicol acetyltransferase, CAT) driven by the HIV LTR is used to determine trans-activation in a cell line constitutively expressing Tat. The use of a parallel ELISA system to determine effects on expression of CAT and of the neomycin phosphotransferase (NPT) marker gene effectively eliminated sample variability caused by cumulative processing errors or cell culture conditions. In addition the use of cationic liposome-mediated transfection minimized delay between DNA treatment that initiates trans-activation and addition of inhibitors, thereby eliminating background expression levels in treated samples. The assay has the potential to discriminate between inhibition of trans-activation and nonspecific effects such as inhibition of transfection and cytotoxicity. It has been adapted to a 96-well format suitable for high-**throughput screening** of natural products and synthetic chemicals.
SO AIDS research and human retroviruses, **(1993 Sep)** 9 (9) 861-7.
Journal code: 8709376. ISSN: 0889-2229.
AB . . . and nonspecific effects such as inhibition of transfection and cytotoxicity. It has been adapted to a 96-well format suitable for high-**throughput screening** of natural products and synthetic chemicals.

L3 ANSWER 12 OF 18 MEDLINE on STN
AN 94063506 MEDLINE
DN PubMed ID: 8244023
TI Inactivation of a yeast transactivator by the fused HIV-1 proteinase: a simple assay for inhibitors of the viral enzyme activity.
AU Murray M G; Hung W; Sadowski I; Das Mahapatra B
CS Schering-Plough Research Institute, Kenilworth, NJ 07033-0539.
SO Gene, **(1993 Nov 30)** 134 (1) 123-8.
Journal code: 7706761. ISSN: 0378-1119.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; AIDS
EM 199401
ED Entered STN: 19940201
Last Updated on STN: 19940201
Entered Medline: 19940105
AB The human immunodeficiency virus type 1 (HIV-1) proteinase (PR) and its flanking sequences have been fused in frame between the DNA-binding domain

and the transcription-activation domain of the yeast protein, GAL4. As has been shown before with the 3C proteinase of Coxsackie virus B3 (CVB3) [Das Mahapatra et al., Proc. Natl. Acad. Sci. USA 89 (1992) 4159-4162], the GAL4::PR fusion protein retains its GAL4 function, providing the PR is inactive. When PR is active, its autocatalytic activity in the hybrid protein is shown to inactivate the transactivation function of GAL4. This provides a simple assay to monitor PR activity. A dose-dependent effect of a potent PR-specific inhibitor is demonstrated in this system and illustrates the sensitivity of the assay. The assay is used for high **throughput screening** to identify novel inhibitors of the viral PR, and provides a method to generate and analyze mutants and revertants of the PR.

SO Gene, **(1993 Nov 30)** 134 (1) 123-8.
Journal code: 7706761. ISSN: 0378-1119.

AB . . . PR-specific inhibitor is demonstrated in this system and illustrates the sensitivity of the assay. The assay is used for high **throughput screening** to identify novel inhibitors of the viral PR, and provides a method to generate and analyze mutants and revertants of. . .

L3 ANSWER 13 OF 18 MEDLINE on STN
AN 93127267 MEDLINE
DN PubMed ID: 1282742
TI Invertebrate GABA and glutamate receptors: molecular biology reveals predictable structures but some unusual pharmacologies.
AU Darlison M G
CS Institut fur Zellbiochemie und klinische Neurobiologie, Universitats-Krankenhaus Eppendorf, Universitat Hamburg, FRG.
SO Trends in neurosciences, **(1992 Dec)** 15 (12) 469-74. Ref: 59
Journal code: 7808616. ISSN: 0166-2236.
CY ENGLAND: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 199302
ED Entered STN: 19930226
Last Updated on STN: 19960129
Entered Medline: 19930211
AB Determination of the sequences of invertebrate gamma-aminobutyric acid (GABA)-gated and glutamate-gated receptor/ion channels, through the application of recombinant DNA methods, is not just an academic exercise to effect evolutionary comparisons with the sequences of the corresponding vertebrate receptors. The isolation of DNA clones would provide the tools to investigate the exact locations and functional properties of these neurotransmitter receptors within simple nervous systems. In addition, since GABA receptors, at least, have been suggested to be the targets of certain pesticides, the availability of invertebrate receptor cDNAs might provide the agrochemical industry with the basis for 'high-**throughput' screening** methods for novel pesticidal compounds. Recently, the isolation of molluscan and Drosophila GABA receptor and glutamate receptor cDNAs, and the pharmacological properties of a GABA receptor expressed from one of these clones, have been reported. These studies should stimulate further research into the electrophysiology and pharmacology of native invertebrate ion channel proteins.
SO Trends in neurosciences, **(1992 Dec)** 15 (12) 469-74. Ref: 59
Journal code: 7808616. ISSN: 0166-2236.
AB . . . the targets of certain pesticides, the availability of invertebrate receptor cDNAs might provide the agrochemical industry with the basis for 'high-**throughput' screening** methods for novel pesticidal compounds. Recently, the isolation of molluscan and Drosophila GABA receptor and glutamate receptor cDNAs, and the. . .

L3 ANSWER 14 OF 18 MEDLINE on STN
AN 93061708 MEDLINE
DN PubMed ID: 1435068
TI A simple method for measurement of phosphoramidon-sensitive endothelin converting enzyme activity.
AU Matsumura Y; Umekawa T; Kawamura H; Takaoka M; Robinson P S; Cook N D; Morimoto S
CS Department of Pharmacology, Osaka University of Pharmaceutical Sciences, Japan.
SO Life sciences, **(1992)** 51 (20) 1603-11.
Journal code: 0375521. ISSN: 0024-3205.
CY ENGLAND: United Kingdom

09758917

DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199212
ED Entered STN: 19930122
Last Updated on STN: 20000303
Entered Medline: 19921204
AB We have developed a rapid and convenient assay for measurement of the action of endothelin (ET) converting enzyme (ECE) using the scintillation proximity assay (SPA) principle. On incubation of [125I]big ET-1 at 37 degrees C for 0.5-6 hr with an enzyme preparation, the reaction was terminated by the addition of an ET-1-specific antibody formulated in a buffer designed to shift the pH to alkaline. The antibody was allowed to come to equilibrium for 1 hr at room temperature and the amount of ET-1 produced, detected in a single step by the addition of protein A SPA beads. Using this assay, ECE activities of enzyme preparations obtained from porcine cultured endothelial cells and rat lung were clearly detected. These activities were inhibited by phosphoramidon in a concentration-dependent manner. The SPA based assay is homogeneous requiring no separation steps and takes a half day to complete. This method is therefore suitable for the high **throughput screening** of potential ECE inhibitors.
SO Life sciences, **(1992)** 51 (20) 1603-11.
Journal code: 0375521. ISSN: 0024-3205.
AB . . . homogeneous requiring no separation steps and takes a half day to complete. This method is therefore suitable for the high **throughput screening** of potential ECE inhibitors.

L3 ANSWER 15 OF 18 MEDLINE on STN
AN 92170548 MEDLINE
DN PubMed ID: 1793017
TI Development of high-throughput radioligand binding assays for interleukin-1 alpha (IL-1 alpha) and tumor necrosis factor (TNF-alpha) in isolated membrane preparations.
AU Maloff B L; Delmendo R E
CS Pharmacology Services, Panlabs, Inc., Bothell, WA 98011.
SO Agents and actions, **(1991 Sep)** 34 (1-2) 132-4.
Journal code: 0213341. ISSN: 0065-4299.
CY Switzerland
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199203
ED Entered STN: 19920417
Last Updated on STN: 19970203
Entered Medline: 19920331
AB Cytokine binding has been studied in a variety of intact cells, and in isolated receptor preparations. Each approach is associated with limitations with regard to screening large numbers of samples on a repetitive basis. In order to provide a more reproducible system of screening for compounds which modify IL-1 alpha and TNF-alpha binding, we have developed isolated membrane preparations for studying agents which can alter the association of these ligands with their receptors. These results demonstrate IL-1 alpha binding to BALB/c 3T3 cell membranes and TNF-alpha binding to HeLa S3 cell membranes, and indicate that this is a viable approach to high-**throughput screening**.
SO Agents and actions, **(1991 Sep)** 34 (1-2) 132-4.
Journal code: 0213341. ISSN: 0065-4299.
AB . . . 3T3 cell membranes and TNF-alpha binding to HeLa S3 cell membranes, and indicate that this is a viable approach to high-**throughput screening**.

L3 ANSWER 16 OF 18 MEDLINE on STN
AN 91359198 MEDLINE
DN PubMed ID: 1886076
TI Complement C5a receptor assay for high **throughput screening**.
AU Harris S R; Garlick R K; Miller J J Jr; Harney H N; Monroe P J
CS E.I.Du Pont de Nemours, Biotechnology Systems Division, Billerica, MA 01862.
SO Journal of receptor research, **(1991)** 11 (1-4) 115-28.
Journal code: 8008358. ISSN: 0197-5110.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals

09758917

EM 199110
ED Entered STN: 19911027
Last Updated on STN: 19970203
Entered Medline: 19911004
AB The complement C5a receptor on U937 cells, a human histiocytic lymphoma cell line, stimulated with dibutyryl-cAMP have been stabilized for at least 3 months at a dilute, ready to use concentration. [125I]-Bolton Hunter labeled C5a, (recombinant, human) has been prepared by reverse phase HPLC to 2200 Ci/mmol. Using a filtration binding assay the Kd from receptor saturation analysis is 10-40 pM and there are 50,000-100,000 receptor sites per cell. These reagents have permitted the development of a reliable, reproducible and convenient drug screening assay, in kit format, for compounds acting at the C5a receptor.
TI Complement C5a receptor assay for high **throughput screening.**
SO Journal of receptor research, **(1991)** 11 (1-4) 115-28.
Journal code: 8008358. ISSN: 0197-5110.

L3 ANSWER 17 OF 18 MEDLINE on STN
AN 91219319 MEDLINE
DN PubMed ID: 1850826
TI Mass receptor screening for new drugs.
AU Burch R M; Kyle D J
CS Nova Pharmaceutical Corporation, Baltimore, Maryland 21224.
SO Pharmaceutical research, **(1991 Feb)** 8 (2) 141-7. Ref: 26
Journal code: 8406521. ISSN: 0724-8741.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 199105
ED Entered STN: 19910623
Last Updated on STN: 19910623
Entered Medline: 19910531
AB Mass receptor screening is capable of identifying drug candidates in large compound libraries. Our laboratory has developed a mass screening technology by standardizing assay protocols that can be transferred from receptor to receptor. The entire operation, from disbursement of compounds to data analysis, is computerized to handle vast numbers of experimental results. The success of this method depends upon strict definitions of compound activity, with rapid elimination of compounds that do not fulfill all criteria. Finally, we approach automation with caution. While certain items, such as automatic harvesters, are essential for high-**throughput screening,** much time can be spent optimizing gadgets instead of gathering data.
SO Pharmaceutical research, **(1991 Feb)** 8 (2) 141-7. Ref: 26
Journal code: 8406521. ISSN: 0724-8741.
AB . . . not fulfill all criteria. Finally, we approach automation with caution. While certain items, such as automatic harvesters, are essential for high-**throughput screening,** much time can be spent optimizing gadgets instead of gathering data.

L3 ANSWER 18 OF 18 MEDLINE on STN
AN 91174330 MEDLINE
DN PubMed ID: 1706569
TI Structure-function studies of HIV reverse transcriptase.
AU Prasad V R; Goff S P
CS Department of Biochemistry and Molecular Biophysics, College of Physicians and Surgeons, Columbia University, New York, New York 10032.
NC 1 U01 AI 24845 (NIAID)
SO Annals of the New York Academy of Sciences, **(1990)** 616 11-21.
Ref: 20
Journal code: 7506858. ISSN: 0077-8923.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals; AIDS
EM 199104
ED Entered STN: 19910512
Last Updated on STN: 19970203
Entered Medline: 19910425
AB The retroviral RT is properly under intensive study as the major target of

antiviral therapy. The enzyme exhibits a number of features that make it an attractive target: it is crucial for viral replication; its RNA-dependent DNA polymerase activity is probably unique to viral replication, or if not unique, is generally unimportant in host cell function; its activities are readily monitored; and powerful lead compounds in the form of nucleotide analogues are already in hand. Our laboratory has been involved in studies to elucidate the structure and function of the HIV-1 RT and to develop a formal genetics of the enzyme. Working with constructs expressing RT in bacteria, we been able to use in vitro mutagenesis to localize functions on the molecule; by coupling mutagenesis with high-**throughput screening** of colonies, we have been able to isolate mutants with specific, rare, phenotypes. We believe that extensions of these efforts will help us to understand the functions of the protein and, coupled to a detailed three-dimensional structure, should facilitate the development of new and better inhibitors.

SO Annals of the New York Academy of Sciences, **(1990)** 616 11-21.
Ref: 20
Journal code: 7506858. ISSN: 0077-8923.

AB . . . in bacteria, we been able to use in vitro mutagenesis to localize functions on the molecule; by coupling mutagenesis with high-**throughput screening** of colonies, we have been able to isolate mutants with specific, rare, phenotypes. We believe that extensions of these efforts. . .

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